

Amendments to the Claims

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Claims 1-2 (Cancelled)

Claim 3 (Currently amended): A method of ~~identifying~~ determining whether a compound ~~that~~ modulates insulin receptor activity, comprising comparing using a processor all or part of the structure of a the compound ~~for modulating insulin receptor activity~~ to all or part of the fitted quaternary structure of insulin receptor or a ~~fragment or~~ derivative thereof to determine whether the compound ~~is likely to interact with the insulin receptor and will~~ modulate insulin receptor activity.

Claim 4 (Currently amended): The method of claim ~~1 or 3~~, further comprising determining whether the compound modulates the activity of the insulin receptor or ~~a fragment or a the~~ derivative thereof having insulin receptor activity in an *in vivo* or *in vitro* assay.

Claim 5 (Currently amended): The method of claim ~~1 or 3~~, wherein the compound comprises an insulin receptor agonist or an IR antagonist.

Claim 6 (Currently amended): The method of claim ~~1 or 3~~, wherein the fitted quaternary structure of insulin receptor comprises substantially the entire fitted quaternary structure of insulin receptor.

Claim 7 (Currently amended): The method of claim ~~1 or 3~~, wherein the comparing step comprises further comprising:

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- a) ~~providing-introducing into~~ a computer program on the computer, the computer program including structural coordinates information defining a ligand binding site conformation including at least one residue from monomer A in Table I 1 and at least one residue from monomer B in Table I 1, the ligand binding site defined by the approximate amino acid distances listed in Table I 1, wherein the program displays the quaternary structure thereof;
- b) comparing the structural coordinates of the compound to the structural coordinates of the ligand binding site and determining whether the compound fits spatially into the ligand binding site and is capable of changing insulin receptor from an inactive conformation to an active conformation or biasing insulin receptor towards an active conformation; wherein the ability to change insulin receptor from an inactive conformation to an active conformation or bias insulin receptor toward an active conformation is predictive of the ability of the compound to ~~agonize-modulate~~ insulin receptor activity by agonizing insulin receptor activity.

Claim 8 (Original): The method of claim 7, further comprising preparing the compound that fits spatially into the ligand binding site and determining whether the compound agonizes insulin receptor activity in an insulin receptor activity assay.

Claim 9 (Currently amended): The method of claim 1 ~~or 3~~, wherein the comparing step comprises further comprising:

- a) ~~providing-introducing into~~ a computer program on the computer, the computer program including structural coordinates information defining a ligand binding site conformation including at least one residue from monomer A in Table I 1 and at least one residue from

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monomer B in Table 1, the ligand binding site defined by the approximate amino acid coordinates listed in Table 1, wherein the program displays the quaternary structure thereof;

b) comparing the structural coordinates of the compound to the structural coordinates of the ligand binding site and determining whether the compound fits spatially into the ligand binding site and is capable of changing insulin receptor from an active conformation to an inactive conformation or biasing insulin receptor toward an inactive conformation; wherein the ability to change insulin receptor from an active conformation to an inactive conformation or bias insulin receptor toward an inactive conformation is predictive of the ability of the compound to modulate insulin receptor activity by antagonizeinsulin receptor activity.

Claim 10 (Original): The method of claim 9, further comprising preparing the compound that fits spatially into the ligand binding site and determining whether the test compound antagonizes insulin receptor activity in an insulin receptor activity assay.

Claim 11 (Currently amended): The method of claim 4 or 3, wherein the comparing step comprises further comprising:

- a) providing-introducing into a computer program on the computer, the computer program including structural coordinates-information defining a cam including at least one residue from the Cam-loop segment in Table 2 and at least one residue from the L1 surface in Table 2, wherein the program displays the quaternary structure thereof;
- b) comparing the structural coordinates of the compound to the structural coordinates of the cam and determining whether the compound interacts with the cam and is capable of changing

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insulin receptor from an inactive conformation to an active conformation or biasing insulin receptor toward an active conformation;
wherein the ability to change insulin receptor from an inactive conformation to an active conformation is predictive of the ability of the compound to modulate insulin receptor activity by agonizing agonize insulin receptor activity.

Claim 12 (Original): The method of claim 11, further comprising preparing the compound that interacts with the cam and determining whether the test compound agonizes insulin receptor activity in an insulin receptor activity assay.

Claim 13 (Currently amended): The method of claim 1 or 3, wherein the comparing step comprises further comprising:

- a) providing introducing into a computer program on the computer the computer program including structural coordinates information defining a cam conformation including at least one residue from the Cam-loop segment in Table 2 and at least one residue from the L1 surface in Table 2, wherein the program displays the quaternary structure thereof;
- b) comparing the structural coordinates of the compound to the structural coordinates of the cam and determining whether the compound interacts with the cam and is capable of changing insulin receptor from an active conformation to an inactive conformation;
wherein the ability to change insulin receptor from an active conformation to an inactive conformation or bias insulin receptor toward an inactive conformation is predictive of the ability of the compound to modulate insulin receptor activity by antagonizing antagonize insulin receptor activity.

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Claim 14 (Original): The method of claim 13, further comprising preparing the compound that interacts with the cam and determining whether the test compound antagonizes insulin receptor activity in an insulin receptor activity assay.

Claim 15 (Currently amended): The method of ~~any of claims 1 or 3~~, wherein the insulin receptor is bound to insulin

Claims 16-18 (Cancelled)

Claim 19 (New): The method of claim 3, wherein the fitted quaternary structure of insulin receptor is determined at a resolution of at least 3 Angstroms within the domains of the quaternary structure and at least 5 Angstroms between domains of the quaternary structure.